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Letter to the Editor

Flybrain, an On-Line Atlas and Database of the Drosophila Nervous System

Flybrain is designed to provide access to a range of anatomical data relevant to the structure and function of the Drosophila nervous system. It can be accessed via the World Wide Web (WWW) from servers in Glasgow (http://flybrain.gla.ac.uk/), Freiburg (http://flybrain.uni-freiburg.de/), and Tucson (http://flybrain.neurobio.arizona.edu/).

Drosophila is a well-established model system for the study of nervous system structure, development, and function. Compared with the brain of even the smallest vertebrate, the Drosophila brain and thoracic ganglia comprise relatively few neurons, perhaps fewer than 200,000 in the adult. Drosophila nevertheless displays a variety of complex behaviors, among which are associative learning (DeZazzo and Tully, 1995), courtship (Hall, 1994), and sophisticated sensorimotor coordination (Götz, 1975; Strauss and Heisenberg, 1993).

Much of what we know of the basic organization of the Drosophila nervous system has been gathered via the techniques of traditional neuroanatomy, e.g., reduced silver staining (Power, 1943), Golgi impregnation (Fischbach and Dittrich, 1989; Hanesch et al., 1989; Stocker et al., 1990), autofluorescence (Heisenberg and Böhl, 1979), dye fills (Wyman et al., 1984; Strausfeld and Singh, 1980; Murphey, et al., 1989), immunohistochemistry (Nässel, 1993), and electron microscopy (Technau and Heisenberg, 1982; Meinertzhagen and O'Neil, 1991). What Drosophila also provides is an array of genetic tools with which we can probe brain organization and function to an extent not yet possible for most other organisms.

Conspicuous among the new visualization techniques is enhancer trapping, notably the P[GAL4] system (Brand and Perrimon, 1993; Kaiser, 1993; Yang et al., 1995 [this issue of *Neuron*]), and more generally any method that allows particular subsets of cells to be picked out on the basis of reporter gene expression. Here the small size of Drosophila is turned to advantage, since we can visualize a whole brain hemisphere or ganglion as a single image by confocal microscopy. Stacks of confocal sections reveal structure layer by layer and are easily built into three-dimensional representations, without the need for fiducial reference points. Besides providing a means of visualizing neuronal organization, the P[GAL4] system has the considerable advantage of enabling manipulation of identified cells in the living organism, and can thus allow direct correlation of brain structure with function (Ferveur et al., 1995; O'Dell et al., 1995 [this issue of *Neuron*]).

All told, there is a considerable pool of valuable neuroanatomical information already in existence, and it is being added to on a regular basis. Much information fails to enter the published literature, however, at least in part because conventional media are unsuitable for full documentation of image-intensive data. A timely solution to the problem is offered by the WWW. Though still an emerging technology, the WWW provides, for the first time, a platform capable of sharing image data both cheaply and efficiently. It can display not only single images but also animations such as rotating three-dimensional representations. All commonly used desktop computers, regardless of manufacturer, are capable of accessing the WWW, in most cases without additional specification and using freely available software. The single proviso is an ethernet connection.

Flybrain represents a first step toward a WWW-based neuroanatomy atlas and database for Drosophila. It is presently restricted to the adult brain and is structured as follows. The first few levels of Flybrain constitute a Basic Atlas, intended to provide a guide to some of the major structural elements of the brain. The Basic Atlas begins with schematic representations of the brain from a variety of aspects. By clicking the cursor on an anatomical domain of interest, the user embarks on a tour that describes that domain in the context of images obtained by a range of different visualization techniques (see Figure 1). Image types are as follows:

Serial frontal sections prepared by the reduced silver technique are each displayed against a common coordinate system. Specific structures (tracts, neuropils, cell body groups, and receptor types) are labeled using terms that have become standard for Drosophila and other insects (Heisenberg, 1980; Mobbs, 1987; Strausfeld, 1976). Horizontal and sagittal series will be added. There is also a complete series of horizontal autofluorescence sections, annotated with respect to the major anatomical subdivisions. These will be joined by frontal and sagittal series. Each section series is presented in a common format, and each image is accompanied by descriptive text from which hypertext links are made to other relevant data.

Among such links are enhancer-trap images that reveal specific anatomical subdomains, or cell groupings, in isolation, and Golgi impregnations that illustrate specific aspects of neuronal morphology. A library of particularly informative Golgi impregnations will be added during the next year. The aim is to provide the user with a general overview of how the different parts of the brain are constructed and connected, and to facilitate interpretation of mutant phenotypes. Extension to aspects of the nervous system other than the adult brain is planned.

Beneath the Basic Atlas is a compendium of more specific data, at present largely restricted to enhancer-trap images but intended to provide a home for all manner of neuroanatomical data, usually in the form of one or more image files linked to each other and to other relevant data via a hypertext description. Users can peruse indices of

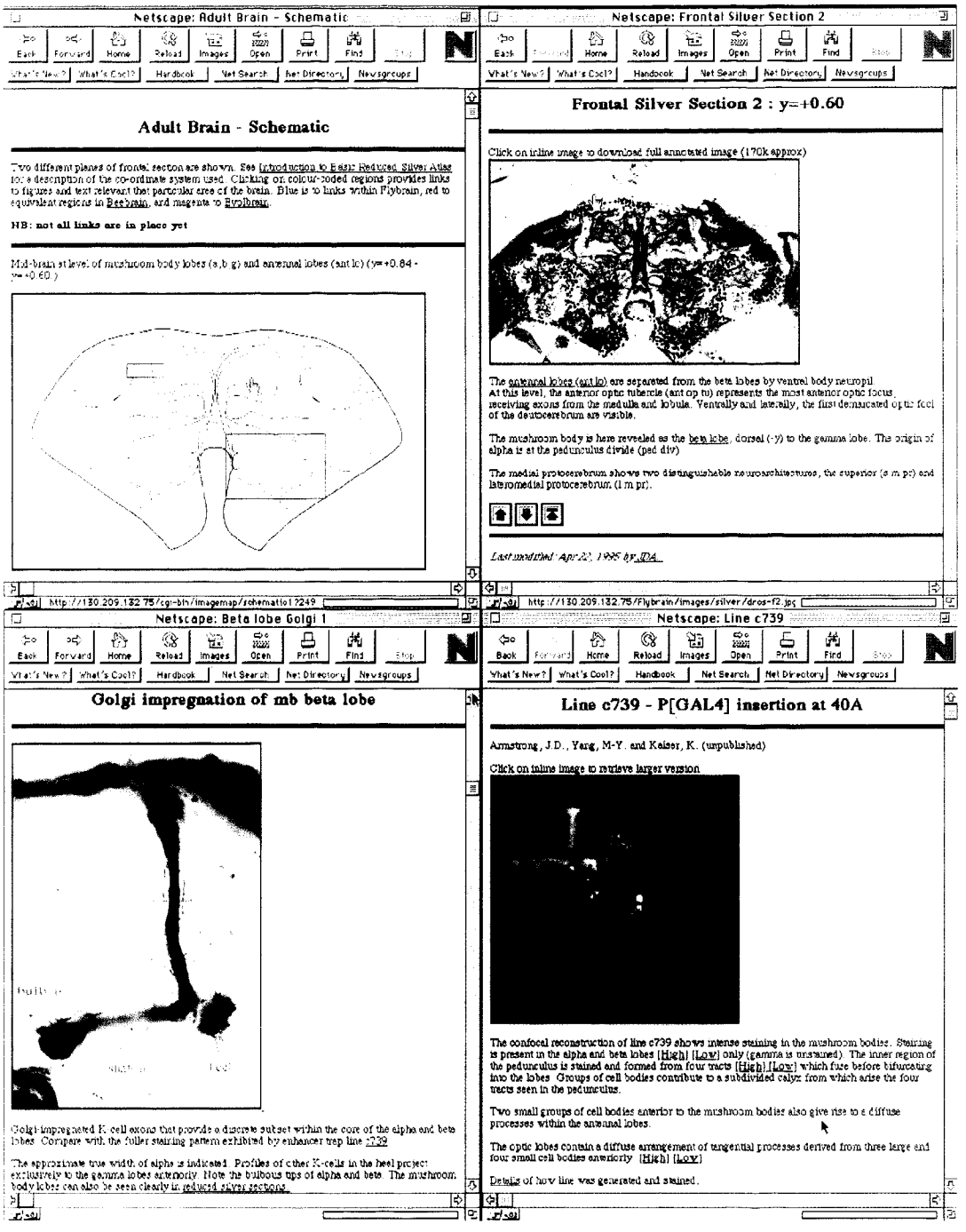

Figure 1. Segments of Four Linked Flybrain Pages

Top left is a schematic representation of a frontal slice though the adult Drosophila brain in a plane that includes the mushroom bodies and antennal lobes. It is a hypertext image map. Clicking on a boxed region links to other data files concerning the anatomical structure of interest. Thus, clicking in the region designated β lobe (of the mushroom body) links to a corresponding reduced silver section (top right). Clicking on the in-line silver section downloads a large-format annotated image aligned with respect to a coordinate system (not shown). A textual description of the silver section contains various hypertext links. Clicking on beta lobe links to a relevant Golgi impregnation and associated text (bottom left). Clicking within the latter links to a three-dimensional view of staining in P[GAL4] enhancer-trap line c739.

specific image types and perform a variety of text-based searches. Subject areas will include expression patterns of Drosophila genes and regulatory elements, histochemical and immunohistochemical staining patterns, specific anatomical structures, genetic variants, electron micrographs, activity mapping data, etc. Some examples are already present, and more extensive data are being incorporated.

We hope that this more specialized component of Flybrain will serve an ancillary function to conventional media, allowing presentation of pertinent data beyond the scope of a typical length journal article (e.g., via an accession number). An editorial board will oversee database organization and management. Submitted data will be subject to peer review and will be citable, and it will be a condition of inclusion that Drosophila lines be made freely available to the scientific community. More details concerning these aspects of Flybrain are available on-line. We have also provided space for poster-like presentations, where preliminary data can be presented and discussed in an informal fashion.

Each Flybrain image is provided at more than one resolution. The smallest version is an in-line image, in all cases large enough to show at least some relevant detail. Clicking on the in-line image downloads a higher resolution version. In the future, we will provide a pyramid of representations to suit several screen sizes and to allow for a range of transfer speeds. Speed of access also depends on proximity to a server. Flybrain can currently be accessed from servers in Glasgow (http://flybrain.gla.ac.uk/), Freiburg (http://flybrain.uni-freiburg.de/), and Tucson (http://flybrain.neurobio.arizona.edu/). Flybrain uses standard software throughout, however, and will thus be amenable to local mirroring where required.

In designing Flybrain, we have kept in mind the desirability for transparent links to other databases. Particularly important will be links to FlyBase, the general database of the Drosophila genetics community (Ashburner and Drysdale, 1994; The FlyBase Consortium, 1994). A first step will be reciprocal hypertext pointers linking image files in Flybrain with reports on relevant genes in FlyBase. Integration will be facilitated by a common vocabulary of terms. We also hope that Flybrain will serve as the seed for other databases concerning structure and function of insect nervous systems (e.g., "Beebrain," "Locustbrain," and "Mothbrain"). In addition to their utility for specific user groups, such a network of databases would be of considerable benefit for comparative studies of nervous system organization. Thus, a user interested in the mushroom bodies of Drosophila would be able to access data concerning similar brain centers in a range of insects. Hypertext guides to evolutionary issues might give rise to meta-level atlases (e.g., "Evolbrain").

Flybrain was recently adopted as the format for the atlas/database of the Flybrain Project, an international collaboration within the Drosophila neuroanatomy community (see link from Flybrain front page). Flybrain will now develop according to the interests of this wider user group, both by extension of the Basic Atlas and by the accumulation of research-oriented data. By linking the available information in different ways, it will be possible to provide tutorials or guides to suit a range of educational and research purposes. Finally, and perhaps most important of all, Flybrain will allow neurobiologists to perceive new relationships between data obtained by a variety of experimental approaches, and thus gain new insights into the workings of the Drosophila nervous system.

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